AMENDMENTS TO THE SPECIFICATION

Amend the paragraph beginning at page 20, line 17, of the specification, as follows.

Figure 4 shows a sequence alignment of the *C. elegans* KAT-1 N-terminal region with homologues from other species (SEQ ID NOS:4-11). The asterisk indicates residues that form the catalytic site of the enzyme. The position of missense mutations is identified as are the DNA base change and allele names (e.g. mg368).

Amend the paragraph beginning at page 20, line 22, of the specification as follows.

Figure 5 shows a sequence alignment of the *C. elegans* KAT-1 C-terminal region with homologues from other species (SEQ ID NOS:12-19). The asterisk indicates residues that form the catalytic site of the enzyme. Missense mutations, DNA base changes, and allele names are indicated (e.g. mg368).

Amend the paragraph beginning at page 21, line 4, of the specification, as follows.

Figures 7A-7F show the expression pattern and focus of action of KAT-1, a peroxisomal 3-ketoacyl-coA thiolase. Figure 7A is schematic representation of the KAT-1 protein structure showing the relative position of mutations and the corresponding changes in amino acid sequence. Figures 7B-7E are photomicrographs showing *kat-1*p::GFP expression. Figure 7B shows expression of *kat-1*p::GFP in the intestine of a 3-fold stage embryo. Figure 7C shows expression of *kat-1*p::GFP in the intestine of an L1 larvae. Figure 7D shows expression of *kat-1*p::GFP in the intestine, pharynx, and body wall muscle of an L4 larvae. Figure 7E shows tissue specific rescue of *kat-1* in *kat-1(mg368) tub-1(nr2004)* worms. *kat-1* cDNA was driven by *kat-1*, *ges-1* or *tub-1* promoter and the level of Nile red fluorescence in 2-day old adult worms of two independent transgenic lines was quantified. The level of fluorescence of *kat-1(mg368) tub-1(nr2004)* worms is set at 100% and the percent change in fluorescence in transgenic worms is shown. At least two independent experiments were performed and error bars indicate the standard error of the mean. The number of worms examined is as follows: *kat-1 tub-1* N=30, *mgEx681* N=31, *mgEx682* N=31, *mgEx683* N=28, *mgEx684* N=28, *mgEx685* N=29, *mgEx686* N=28. Figure 7F shows a sequence alignment of KAT-1 and its orthologues, human ACAA1 and yeast Pot1p (SEQ ID NOS:20-22). The conserved catalytic residues (GHP) in each of the orthologs are marked with an asterisk.

Amend the paragraph beginning at page 22, line 17, of the specification, as follows.

Figures 13A-13F show the cloning and characterization of *bbs-1*. Figure 13A is a schematic representation of the BBS-1 protein structure showing the position of the mutant allele *mg409*. Figure 13B is a graph showing the quantification of Nile red fluorescence in 2-day and 6-day old adult worms. The level of fluorescence in wild-type worms is normalized to 1 and the fold change in fluorescence in mutant worms is shown. At least two independent experiments were performed and error bars indicate standard deviation. The number of 2-day old adult worms examined is as follows: wild-type N=34, *kat-1(mg368)* N=30, *bbs-1(mg409)* N=32, *bbs-1(mg409)*; *kat-1(mg368)* N=36, *bbs-1(mg409)*; *tub-1(nr2004)* N=35. The number of 6-day old adult worms examined is as follows: wild-type N=35, *kat-1(mg368)* N=31, *bbs-1(mg409)* N=33, *bbs-1(mg409)*; *kat-1(mg368)* N=31, *bbs-1(mg409)*; *tub-1(nr2004)* N=24. Figure 13C is a graph that depicts the quantification of Nile red fluorescence in 6-day old adult worms. The level of fluorescence in wild-type worms is normalized to 1 and the fold change in fluorescence in mutant worms is depicted. Two independent experiments were performed and the error bars indicate the standard deviation. The number of worms examined is as follows: wild-type N=34, *bbs-1(mg409)*; *kat-1(mg368)* N=25, *bbs-1(mg409)*; *kat-1(mg368)*; *mgEx687* N=26, *kat-1(mg368)*; *mgEx688* N=25. Figure 13D is a series of photographs of worm

culture plates that illustrate the wild-type phenotype of N2 worms, the dwelling phenotype of *bbs-1(mg409)*; *kat-1(mg368)* mutant worms, and the rescue phenotype of the double mutant worms expressing transgene, *mgEx687*, which restored wild-type *bbs-1* activity. Pictures were taken 20 hours after a single 1-day old adult worm was transferred onto a plate with abundant food and incubated at 20°C. Figure 13E is a pair of photomicrographs that show the localization of BBS-1::GFP to the transition zone of a phasmid neuron. The left panel shows the dendrite and cilium visualized with DiI staining, and the right panel shows the same worm visualized by Nomarski optics. Figure 13F shows the alignment of *C. elegans* BBS-1 and its human counterpart (SEQ ID NOS:23 and 24).

Amend the paragraph beginning at page 24, line 4, of the specification, as follows.

Figures 16A -16C depict the characterization of the *egl-4(mg410)* molecular lesion. Figure 16A is a schematic diagram showing the exon intron structure of F55A8.2a, F55A8.2b, F55A8.2c, and F55A8.2d. Figure 16B shows the nucleic acid and amino acid sequences in the region of the mutation (SEQ ID NOS:25-28). Figure 16C is a gel showing the results of an Ssp1 restriction digest of PCR amplified genomic DNA, extracted from wild-type and *mg410* worms, flanking the mg410 mutation. The mg410

mutation creates an additional SspI restriction site.

Amend the paragraph beginning at page 24, line 12, of the specification, as follows.

Figure 17A is a schematic diagram showing EGL-4 functional domains. Figure 17B shows the amino acid sequence of the consensus sequence for the kinase substrate motif and the pseudo-substrate motif ~~in~~ (SEQ ID NOS:29 and 30). Figure 17C shows the amino acid sequence of the pseudo-substrate motif in *egl-4* loss of function and gain-of-function, *mg410*, mutants (SEQ ID NOS:31 and 32).

Amend the paragraph beginning at page 24, line 19, of the specification, as follows.

Figure 19 is an alignment of *C. elegans* EGL-4 and its human ortholog (SEQ ID NOS:33 and 34). Identical amino acid residues are indicated with black shading and conservative substitutions are indicated with gray shading.

Amend the paragraph beginning at page 47, line 1, as follows.

For the *kat-1*p::GFP construct, PCR products that encompass the *kat-1* 5' regulatory region (1.5kb) and the GFP-coding region plus *unc-54* 3'UTR from pPD95.79 (2kb) were assembled using a recombinant PCR method. For tissue specific rescue of *kat-1*, a *kat-1* cDNA (provided by ~~Mark. Vidal~~ Mark Vidal) was first subcloned into pPD49.78, in order to append the *unc-54* 3'UTR to its 3' end. The following promoters were amplified from N2 genomic DNA: *kat-1* (1.5kb), *ges-1* (2.5kb) (Aamodt et al., 1991) and *tub-1*(1.4kb). The primer sequences defining the 5' end of the promoters used are as follows:

kat-1, 5'-acctacgtcgcaagaatgaaac-3' (SEQ ID NO:1);

ges-1, 5'-ttaacaaggacgatggtccag-3' (SEQ ID NO:2);

tub-1, 5'-gaaaattccgctaaacttaaac-3' (SEQ ID NO:3).

Each promoter fragment encompassed sequence immediately 5' to the start codon of the respective gene. The promoter fragments were then fused to the *kat-1* cDNA and *unc-54* 3'UTR by recombinant PCR.

Please insert the Sequence Listing submitted with the concurrently filed Sequence Statement at the end of the specification.